DEFEAT-polypharmacy: Deprescribing anticholinergic and sedative medicines Feasibility Trial in Residential Aged Care Facilities

Nagham Ailabouni[1], PhD, Senior Fellow

Dee Mangin, Professor[2]

Prasad S. Nishtala[3], Reader

1) School of Pharmacy, University of Otago, Dunedin, New Zealand

2) University of Otago, Christchurch and David Braley Nancy Gordon, Chair in Family Medicine, McMaster University, Canada

3) Department of Pharmacy and Pharmacology, University of Bath, Building 7 West, Bath BA2 7AY, United Kingdom

Address correspondence to:

Nagham Ailabouni
School of Pharmacy
University of Otago
Dunedin, New Zealand
Email: nagham.ailabouni@otago.ac.nz

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Introduction

Prescribing medicines is practiced routinely and is often driven by test results, symptoms or a confirmed disease diagnosis [1], with some prescribers considering continuing prescribed medicines as the safer course of action [2]. However, older adults with co-morbidities may benefit to a lesser degree from medicines due to competing risks of negative health outcomes, including medication-related harms and death before benefits can be accrued [3].

Deprescribing, the supervised withdrawal of unnecessary medications to minimize polypharmacy [4] is linked to potential health gains including improvements in cognition [5], reduction in falls and hip fractures [6, 7], improved medication adherence [8] and other positive health outcomes [5-7, 9]. However, this is not perceived as an easy process and the challenges of reviewing medication are many and transverse multiple healthcare processes [10].

With ever-increasing demands on the healthcare system by an ageing population worldwide [11, 12], it is important to address the challenges of implementing deprescribing in a safe and feasible manner. In New Zealand, these challenges include time constraints, fear of consequences and lack of accessibility to guidelines and processes that empower physicians to deprescribe medication [10, 13]. The best approach to implementing deprescribing, addressing major deprescribing barriers, is not yet clearly understood [14]. This study examines the feasibility of deprescribing anticholinergics and sedatives in older people in residential care facilities using a pharmacist-led intervention.

These medicines are commonly prescribed [15] and are associated with both cognitive and physical functioning impairment [16]. Several tools can be used to measure the anticholinergic and sedative burden [17]. We chose the Drug Burden Index (DBI) as this has been validated in several older populations worldwide [18] and studies have shown a correlation between increasing DBI and worse patient outcomes, including mortality, cognition, frailty and falls [18]. Each additional unit of DBI exposure has a negative effect on older people's physical function similar to that of three additional comorbidities [19]. Therefore, the DBI provides a useful tool to help inform improved prescribing patterns.

Aim of the study

Our overarching aim was to test the feasibility of a collaborative pharmacist-led medication review with General Practitioners (GPs). The review utilised a patient-centred approach to implement deprescribing recommendations based on peer-reviewed deprescribing guidelines. We hypothesise that DBI could be reduced in residential aged care facilities (RACFs) utilising this intervention.

Ethics Approval

Ethics approval was obtained from the Health and Disability Ethics Committee (16/NTA/61).

Methods

This trial's methods are outlined in a published protocol [20]. The trial was registered in the Australasian Clinical Trials Registry (ACTRN12616000721404). The Template for Intervention Description and

Replication (TIDieR) checklist was used when designing the study **(Supplementary Table 1)**. The study is diagrammatically represented using CONSORT Reporting Guidelines in **Supplementary Figure 1** [21].

Study Design

A single group (pre- and post- comparison) feasibility study was carried out in people aged 65 years and older living in a residential care setting. **Figure 1** provides an overview of the intervention. Participants were recruited from three RACFs in New Zealand.

Power and sample size

To detect a clinically significant difference in the primary outcome (reduction in DBI total score of 0.5 or more) with 80% power and alpha of 0.05, the total sample size required was 72 participants [20]. This effect size is derived from a study conducted in Australian RACFs that aimed at decreasing the DBI load [22]. Power calculations were generated using Stata 13.1 (Copyright 1985-2013 StataCorp LP).

Inclusion and Exclusion Criteria

Participants who are aged ≥ 65 years who are prescribed at least one anticholinergic or sedative medicine (i.e. DBI≥0.5) were included. The target medicine list was adapted from Hilmer *et al.* [23]. Those who were expected to have a limited life expectancy, receiving palliative care or those admitted for hospice care were excluded.

Recruitment and consent

The RACF's e-prescribing program was screened for residents who fulfilled the inclusion criteria. Of these, nurse(s) determined residents who were able to provide consent. The pharmacist provided these residents with a participant information sheet and consent form. For residents with cognitive impairment; the pharmacist gained consent via their enduring power of attorney (EpoA). Recruitment continued for 4 months.

Intervention

A collaborative pharmacist-led medication review with GPs was employed, as this model has been shown to improve the success of deprescribing [24].

Step 1: Medical history

The InterRAI-Long Term Care Facility (LTCF) is a comprehensive assessment database system, utilised in RACFs internationally and in New Zealand to standardise the evaluation of older people's complex care needs. It is used routinely to collect data regarding patients' medical and functional status [25]. We used this along with clinical notes, to collect participants' data. The reliability of InterRAI-LTCF has been tested and shown to meet the standard cut-offs for acceptable reliability [26].

Step 2: Initial consultation

After completing an initial consultation, potential medicine(s) that could be deprescribed were discussed and any patient concerns were noted. For participants with diminished cognition, the pharmacist invited a nurse and/or the EpoA to help facilitate communication. When a response from the participant was not possible, the test was recorded as 'not assessed' and the information was gathered from clinical notes.

Step 3: Deprescribing medication review

The deprescribing medication review utilised peer-reviewed deprescribing guidelines developed as part of the principal investigator's doctoral studies [20]. When these target medicines are reduced/discontinued, adverse drug withdrawal effects (ADWEs) may develop including increased agitation, pain, confusion, or disturbed sleep patterns [27]. Therefore, it is important to slowly taper these medicine(s) whilst monitoring the participant. Medicine(s) that can be deprescribed were discussed with each participant and their consent to deprescribe was sought. When participants disagreed, these recommendations were removed from the review ensuring this is a patient-centred approach. Similarly, for participants with diminished cognition, approval for deprescribing recommendations was sought from their EpoA before putting forward these recommendations to the GP. The GP reviewed, endorsed, adjusted or rejected the recommendations. Any reasons for rejection were recorded.

Step 4: Medication management plan

We developed a medication management plan (MMP) that included individualised tapering and monitoring recommendations for the participant, GP and residential care staff. The MMP listed the medicines to be deprescribed, the recommended order of deprescribing, specific tapering guidance, anticipated ADWEs, monitoring and appropriate management options for withdrawal effects. The participant and/or their relative/representative were provided with a copy of the plan. The GP then initiated deprescribing and all other aspects of follow up care.

Step 5: Monitoring and follow-up

After the cessation/dose reduction of the first target medicine, participants were monitored twice weekly by the pharmacist for ADWEs. If none were reported, dose reduction continued until the medicine was stopped. The participant continued to be reviewed twice weekly for a further two weeks, and if symptoms were stable, the dose of the next target medication was reduced until it was ceased. This process was repeated until all target medicines were withdrawn. The participant was monitored by the pharmacist on a weekly basis for two more visits and, if stable, no additional visits were conducted. Monitoring also took place independently by nursing staff. GPs were notified if their resident developed an ADWE to facilitate a GP visit and/or re-prescribing of medicine(s) as appropriate.

Data Collection and Analysis:

During the initial consultation, frailty was assessed using the Edmonton Frailty Scale [28], depression was assessed using the Geriatric Depression Scale (GDS) [29], side effects attributed by target medicines were assessed using UKU- Side Effect Rating Scale (UKU-SERS) score [30] and quality of life (QoL) was assessed using EQ-5D-3L [31]. Covariates were collected at baseline (T0), after three months (T1) and after six months (T2) as detailed in the study protocol [20] and **supplementary Table 2**. Data was be stored in a password-protected Excel spreadsheet.

Primary Outcome: The change in the participant's DBI three and six months after the deprescribing intervention had been implemented. PRN 'as required' DBI medicines that had been administered more than once in the past three months were included in the total DBI score. A separate DBI PRN was also calculated.

Secondary Outcomes: An in-depth description of these outcomes is included in the study protocol [20] and in **Supplementary Table 3.**

Statistical Methods

Data were analysed on an intention-to-treat basis. R was used for statistical analyses [32]. The primary outcome of change in the DBI at three and six months was assessed with a Wilcox-signed Rank Test (WSR). Depending on the distribution of secondary outcome data, either a paired t-test or WSR were used for analysis at three and six months. Fisher's exact test was used to analyse the uptake of deprescribing recommendations.

Results

In total, 46 of 65 potentially eligible participants consented and were enrolled **(Figure 2)**. Our study attrition rate was 8.7%, with four residents passing away for reasons unrelated to the deprescribing intervention. Participant demographics are summarised in **Table 1**. Almost half of participants had a high falls risk (41%) and the majority (93%) had polypharmacy, which was defined as the prescription of five or more medicines [33].

In total, the pharmacist suggested 45 deprescribing recommendations among 46 residents. Of these, 82% were agreed upon by the residents' GP and 96% were agreed upon by the resident or the resident's relatives/family **(Table 2)**. In total, 33 recommendations (72%) were implemented (p=0.01; Fisher's exact test); and the medicines were re-prescribed by the GP in only five instances (15.2%). Deprescribing processed could not be completed in 13 residents (28.2%) due to mood changes, increased pain levels or overall health deterioration.

Table 3 illustrates the analysis of primary and secondary outcomes three months after deprescribing and **Table 4** illustrates the analysis six months after deprescribing. Participant's overall DBI and DBI PRN were significantly less three months after deprescribing. Six months after deprescribing **(Table 4)**, the DBI remained statistically significantly decreased by a median of 0.34. Six months after deprescribing, total regular medicines were reduced statistically, by a mean difference of 2.13 medicines per patient, among patients were deprescribing was initiated. However, the use of PRN medicines remained the same. Falls risk was determined using an in-house falls risk assessment tool utilised by most RACFs in New Zealand and 41% of residents had a high falls risk at the time of recruitment. This remained the same six months after deprescribing. Fall rate defined as the number of falls in the past 90 days was determined by interRAI and showed a statistically significant reduction. Frailty, assessed using the Edmonton Frailty Scale, also showed a significant decrease; the mean difference was 1.35 ($p<0.05$, 95%, CI: -2.22; -0.48). QoL assessed using EQ-5D-3L was not significantly different six months after deprescribing.

Six months after deprescribing, total regular medicines were reduced statistically, by a mean difference of 2.13. However, the use of PRN medicines remained the same. Fall rate was determined using falls data recorded in interRAI, where the number of falls that occurred in the past 90 days was noted. Falls risk was determined using an in-house falls risk assessment tool utilised by most RACFs in New Zealand. Forty-one percent of residents had a high falls risk at the time of recruitment. This remained the same six months after deprescribing. On the other hand, the participants' number of falls statistically significantly dropped.

Frailty assessed by the Edmonton Frailty Scale also dropped by a mean difference of 1.35 ($p<0.05$, 95%, CI: -2.22; -0.48). QoL assessed by EQ-5D-3L did not improve six months after deprescribing.

Participants reported significantly less adverse effects of psychotropic medication at 3 and 6 months after deprescribing than at the time of recruitment. Psychiatric, neurological, autonomic and other adverse effects dropped significantly 3 and 6 months after deprescribing. Psychiatric adverse effects decreased by a mean difference of 1.8 ($p<0.05$; 95%, CI: -2.6; -1.0) 3 months after deprescribing, and by a mean difference of 2.24 ($p<0.05$; 95%, CI: -3.63; -1.12) after 6 months of deprescribing.

Potential adverse drug reactions (ADRs) had decreased by a mean difference of 2.8 three months after deprescribing ($p<0.05$; 95%, CI: -4.00; -1.64) and by 4.24 after six months ($p<0.05$; 95%, CI: -5.66; -2.83). We found no change in cognition three or six months after deprescribing. However, participants' levels of depression scored using the GDS significantly improved (Median difference: -2; $p<0.05$).

Discussion

This feasibility study implemented a targeted systematic intervention of deprescribing anticholinergic and sedative medicines using a five-step patient-centred approach. We aimed to explore the feasibility of a pharmacist-led deprescribing intervention that can address some of the major barriers associated with deprescribing, and our results support the feasibility of such an approach [20].

The findings from this feasibility trial support existing research that shows that despite the challenges, rationalising the use of medicines in older people through deprescribing is feasible and may realise potential benefit [27]. Our results are consistent with other studies that illustrate that deprescribing contributes to an overall reduction in pill burden [5, 9, 27].

Most eligible patients or their EpoAs, consented to participation and overall, 45 recommendations were suggested to the residents' GPs. Eighty-two percent of these were agreed upon by the residents' GP; 72% of them were implemented. Despite previous studies reporting residents' unwillingness to discontinue medicines, we found that the majority of residents and/or their representatives (96%) agreed with the deprescribing recommendations. This finding is echoed in another cross-sectional survey, which showed that most residents (78.9%) reported a desire to stop taking one or more of their medicines [34].

Though not powered to detect a significant difference, this study sheds light on the effect that deprescribing has on participants' DBI scores and relevant patient health outcomes. The statistically significant reduction in DBI scores by 0.34 may support clinical relevance in a larger study; as although in our feasibility study this represents a small decrease, studies have shown an association between increasing DBI and impaired functioning [23, 33, 35, 36].

Participants reported lower depression and frailty scores six months after deprescribing. Cognition, however, did not improve after deprescribing, nor did participants' QoL scores. Our study was not powered to detect these differences and we can only speculate that six months is not long enough to observe such differences, especially in older patients who may suffer from cognitive impairment. However, the lack of QoL deterioration over the period of the study could be a positive finding attributed to deprescribing that ought to be explored in further studies [14].

Psychotropic-related ADEs were reduced six months after the deprescribing intervention. This finding supports existing evidence that the withdrawal of specific medication classes, including benzodiazepines, leads to the reduction of ADRs [15]. There were no adverse events noted as a result of deprescribing. Approximately, fifteen percent of the participants had to have one or more of their deprescribed medicines re-prescribed. Despite this, the overall number of medicines prescribed was reduced significantly. This illustrates that deprescribing was well tolerated, supporting previous research that has shown that frail older people's medication burden can be reduced without any detrimental effects to their health [5, 9].

Strength and Limitations

The study design meant that the participants and outcome assessment were not blinded. However, several outcomes were objective measures, such as the DBI, hence mitigating the risk of assessment. ADWEs were assessed subjectively by the pharmacist and the residential care staff; introducing possibility of bias. The potential that a placebo effect may underpin some changes seen is another limitation that is inherent to pre-post intervention studies. However, this does not affect the study's primary outcome; the change in DBI scores. Time-period effects cannot be ruled out, as controls were not included in the study design.

No restrictions were put in place to prevent medicines being re-prescribed. This pragmatic approach mimics real-life clinical scenarios where medicines are often re-prescribed after being stopped for several, often appropriate, reasons. Despite having a relatively high recruitment rate of 71%, we were unable to recruit the calculated sample size (n=72) due to strict eligibility criteria. We had anticipated this, as other deprescribing studies had shown recruitment could be challenging mainly due to the fear associated with deprescribing medicines [37]. Although our study showed improvement in the majority of outcome measures, six months is not an adequate term to observe changes related to cognitive function.

We found that some participants perceived deprescribing as 'going against' their GPs' initial decision of prescribing the target medicine(s) in question. Re-assuring them that recommendations would be discussed and finalised with and by their GP appeared to support participation in decisions regarding their medicines [38]. Other challenges we encountered included time constraints faced by GPs [39]. Scheduling face-to-face GP appointments for the pharmacist to discuss recommendations was challenging. However, once scheduled, thirty-minute visits were adequate to review recommendations and implement any necessary medicine changes.

Engaging a patient-centred approach was crucial, as the aim of deprescribing is to address patients' health concerns [1] and respect their preferences. This has been shown to significantly improve medication adherence [8]. Utilising a clinical pharmacist to perform the reviews; helped address time constraints faced by GPs [40]. Assuring GPs that residents are receiving adequate monitoring may also have increased the confidence of GPs by diminishing concerns around potentially harmful effects often associated with deprescribing [40].

Conclusion

This study provides important data indicating the feasibility and benefits of reducing anticholinergic and sedative medication in frail older people. The approach used resulted in high uptake of deprescribing

recommendations by both residents and GPs. At six months, deprescribing showed signals of significant benefits across a range of important health outcomes including mood, frailty, and falls and resulted in a smaller number of reported adverse effects. Implementing deprescribing utilising this patient-centred approach appears to be safe and feasible and can yield potential health benefits in older people.

Funding statement

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Conflicts of interest

The author(s) declare no competing interests and are responsible for this report's content.

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295 **Table 1: Social and Demographic Data**

Characteristic	n	%
Sex		
Female	34	74
Male	12	26
Ethnicity		
Caucasian	45	98
Asian	1	2
Falls risk		
Low	14	30
Moderate	13	28
High	19	41
Polypharmacy		
≥5 medicines	43	93
<5 medicines	3	07
Charlson Comorbidity Index (CCI)		
1	2	4
2	6	13
3	18	39
4	13	28
5	5	11
6	2	4
Body Mass Index (BMI)		
Underweight: 18.5-24.9	19	41
Normal: 25-29.9	18	39
Overweight: ≥30	9	20
Activities of Daily Living (ADL)		
0: Independent	16	35
1: Supervision	8	17
2: Limited	8	17
3: Extensive	9	2
4: Maximal	2	4
5: Dependent	3	7
Pain Scale		
0: No pain	19	41
1: Less than daily pain	25	54
2: Daily pain but not severe	5	11
ABS*		
0: No instances of aggressive behaviour	36	78
1	3	7
2	3	7
3	2	4
4	1	2

8	1	2
CHESS*		
0=No health instability	22	48
1=Minimal health instability	12	26
2=Low health instability	6	13
3=Moderate health instability	3	7
4=High health instability	3	7
5=Very high health instability	0	0
EQ-VAS*		
Report < 50	17	37
Reports 50	7	15
Report > 50	22	48

ABS*: Aggressive Behaviour Scale. Scale scores range from 0-12 with higher scores indicative of greater frequency and diversity of aggressive behaviour.
CHESS: Changes in Health, End-Stage Disease, Signs, and Symptoms Scale. EQ-VAS: EQ Visual Analogue Scale.

Table 2: Deprescribing recommendations

Resident number	Number of recommendations put forward to GP	Number of recommendation agreed by the GP	Number of recommendations agreed by resident/resident's family	Deprescribing recommendations put forward to GP with clinical reasoning	Summary	Represcribed	Deprescribed
1	2	2	2	Loratadine: Resident prescribed promethazine as well as loratadine for eczema. Resident however reported that promethazine is more effective at relieving their symptoms. Therefore, the suggestion was made to the GP* to discontinue loratadine and monitor the control of itching symptoms with promethazine alone. GP* agreed with this suggestion. Tramadol: Resident reported feeling sleepy during the day and drifting off to sleep regularly. Reducing her tramadol dose from 100mg SR* BD* to 50mg SR* mane* or BD* could help to increase energy levels during the day, whilst still providing long-acting pain relief.	Loratadine (discontinued) Tramadol (reduced)	N	Y
2	2	1	2	Nortriptyline: Resident suffers from pain that had been well managed with paracetamol. A reduced dose of nortriptyline was therefore thought to be beneficial to improve the resident's energy levels during the day. GP* agreed with this suggestion. Risperidone: Has a past history of paranoid schizophrenia; so continuing risperidone is necessary. However, resident's mood seemed to be well controlled and stable over the past five years; suggested to the GP* to trial reducing the dose from 1mg to 0.5mg. GP had attempted to reduce risperidone dose in the past and this resulted in relapse of symptoms. Therefore risperidone was continued.	Nortriptyline (reduced) Risperidone (continued)	N	Y
3	1	1	1	Quetiapine: Low dose quetiapine prescribed for aggressive behaviour exhibited by resident upon admission into the residential care facility approximately a year and a half prior to assessment date. As resident did not exhibit any recent acts of aggressive behaviour, the suggestion was put forward to deprescribe quetiapine; whilst continue to prescribe this 'as required'. After three months, this change was well tolerated with no relapse of symptoms and the quetiapine did not need to be administered 'as required'. Therefore, it was successfully discontinued.	Quetiapine (discontinued)	N	Y
4	1	1	1	Carbamazepine: A dose reduction from 200mg BD* to 100mg BD* was suggested as resident's epileptic symptoms have been well controlled with no attacks during the entirety of the resident being admitted into the residential care facility (approximately 5 years). The resident had also expressed that they do not believe they require to continue taking this medication. Discussed with GP who agreed and reduced the dose of carbamazepine. Resident passed away on the 24/09/16 due to chest infection	Carbamazepine (discontinued)	N	Y
5	4	2	2	Nortriptyline: Resident prescribed several medicines for neuropathic pain caused by ulcers secondary to Type 2 Diabetes Mellitus. Resident reported feeling drowsy and loss of concentration during the day. This affected their ability to partake in social activities. Suggestion was made to GP* to reduce nortriptyline dose from 50mg to 25mg. GP* agreed. After three months, the dose reduction was well tolerated and GP* decided to discontinue the use of nortriptyline. Zopiclone: Resident had been prescribed this long-term for sleep aid. However, resident still experienced difficulty falling asleep and staying asleep. Attempting to reduce the resident's high drug burden index by reducing/discontinuing nortriptyline that caused sleepiness during the day; was thought to provide the opportunity for better quality sleep at night therefore	Nortriptyline (discontinued) Zopiclone (discontinued)	N	Y

				reducing the reliance on continuing this medication. Resident refused the zopiclone tablet three months after discontinuing nortriptyline, as they felt they no longer needed it and slept well without it. The GP* therefore discontinued zopiclone. Other medicines that were suggested for reduction were tramadol and gabapentin after nortriptyline and zopiclone were successfully deprescribed. However, GP did not want to risk reducing these medicines as resident's pain might not be well managed at lower doses.			
6	4	1	4	Quetiapine: Indication for prescribed low dose quetiapine was not documented and unclear. Therefore, suggestion was made to reduce quetiapine with the aim of completely discontinuing this. GP* agreed. However, resident passed away on 14/04/17 before further tapering of the dose was possible. Resident had a high drug burden index. Other deprescribing recommendations put forward included a step wise approach to reduce the dose of zopiclone, amitriptyline and lorazepam. GP* felt comfortable with reducing quetiapine and was hesitant to reduce other medicines as the resident had been prescribed them for a long time.	Quetiapine (reduced)	N	Y
7	1	0	1	Lamotrigine: At the time of assessment, it seemed appropriate to trial the reduction of lamotrigine as the resident had not suffered from a recent attack. However, shortly after this the patient had a seizure, and due to her moods being chronically low, the decision to continue lamotrigine was made.	Lamotrigine (continued)	N	N
8	1	1	1	Gabapentin: Prescribed many sedative medicines for pain control, including opioids. Discussed with GP* possibility of reducing gabapentin dose and they agreed with this suggestion.	Gabapentin (reduced)	N	Y
9	1	1	1	Risperidone: Prescribed two antipsychotics for schizophrenia and behaviours associated with personality disorder. Discussed with GP* the possibility of simplifying the regimen and they decided that stopping risperidone; whilst continuing olanzapine would be appropriate.	Risperidone (discontinued)	N	Y
10	2	2	2	Morphine: Pain managed well with paracetamol and other medicines. Suggestion made to stop morphine which was taken up by the GP*. Citalopram: Resident has been in good moods for the past six months and does not suffer from chronic depression or low moods on a constant basis. Suggestion to trial discontinuing this was made and the GP* agreed. Resident passed away on 02/05/2017 due to general deterioration in health.	Morphine (discontinued) Citalopram (discontinued)	N	Y
11	1	0	1	Tramadol: Suggested to the GP* to reduce tramadol dose as patient had previously been prescribed this during an acute stage of pain after injuring her foot. However, GP* expressed that he did not want to taper down tramadol at this stage, as he was stopping other cardiovascular medicines at the time.	Tramadol (continued)	N	N
12	1	1	1	Prescribed zopiclone for many years and resident reported they felt dependent on it and was unsure that they require it. Relayed the resident's interest to try and reduce or stop the use of it. GP* agreed to and the dose was reduced from 7.5mg to 3.75mg. Patient tolerated this well. At the three months assessment, the resident did not feel comfortable with completely discontinuing zopiclone and continued taking half a tablet.	Quetiapine (reduced)	N	Y
13	1	1	1	Quetiapine: Prescribed 75mg BD*, to control hallucinations. Resident has not suffered from hallucinations for a considerable time and was exhibiting signs of sedation during the day and loss of concentration. Suggested reducing the dose to 50mg BD* and prescribing 12.5mg 'as required'. GP* agreed with this suggestion. Resident tolerated the reduced dose well and did not require additional administration of 'as required' quetiapine	Quetiapine (reduced)	N	Y
14	1	1	1	Escitalopram: Indication not clearly documented and resident appears to be overall well with consistent good moods. Suggestion to reduce escitalopram dose with the aim of discontinuation was made and GP* agreed to reduce it. GP* did not feel comfortable	Escitalopram (reduced)	N	Y

				discontinuing this completely at the time however, as the resident suffered from other pain related issues.			
15	2	2	2	Amitriptyline: Prescribed 10mg amitriptyline along with several other sedative and anticholinergic medicines. Indication for amitriptyline was unclear and not documented. Resident thought it might have been prescribed for insomnia; albeit she did not consider this to be effective. Therefore, suggested to GP* to discontinue. GP* agreed with this suggestion. Codeine: Prescribed 60mg TDS* with no clear indication. At the time of assessment, resident reported experiencing dizzy spells, feeling light headed and falling out of her wheelchair a week prior to the assessment. As the resident is a one-leg amputee, frail and has a low BMI, slow tapering of codeine was suggested to the GP* to reduce the resident's drug burden index. GP* agreed to both suggestions. However, resident developed diarrhoea as a result of codeine withdrawal and complained from insomnia; so both medicines were re-prescribed by the GP*.	Amitriptyline (reduced, discontinued then re-prescribed) Codeine (reduced then re-prescribed)	Y	N
16	1	1	1	Citalopram prescribed since admission into the residential care facility (approximately five years ago). Suggested trialling reduction from 20mg to 10mg as staff had reported that citalopram 20mg did not seem to lift resident's moods significantly more. After three months of the reduction, resident communicated suicidal thoughts to staff. Therefore, GP* increased citalopram dose again.	Citalopram (reduced then re-prescribed)	Y	N
17	2	2	2	Temazepam: Prescribed upon admission into the residential care facility (approximately two years ago). However, resident has been stable for the past year and expressed that he does not struggle to fall or stay asleep. In fact, the resident enjoys waking up at 4am on a daily basis. Therefore, suggested tapering temazepam dose from 20mg to 10mg with one 10mg tablet being prescribed 'as required' in case resident really requires it. The. GP agreed and tapering was well tolerated and resident did not require the extra temazepam tablet. Venlafaxine: Resident was prescribed a high dose of venlafaxine (375mg). Has suffered from extensive mental health issues; including depression. However, resident reported good moods at time of the assessment and scored 4 on the geriatric depression scale test. Therefore, suggested reducing venlafaxine dose to 300mg (also a simpler medication pill regimen). GP agreed with this suggestion and resident tolerated this well.	Temazepam (reduced) Venlafaxine (reduced)	N	Y
18	0	0	0	Resident suffers from severe pain and chronic depression. On several sedative medicines as well as moclobemide for depression. However, not feasible to discontinue medicines	All medicines continued	N	N
19	1	1	1	Resident prescribed escitalopram 10mg and admitted to not taking the medicine and throwing it out instead for the eight months prior to assessment date. Requested from the GP* to discontinue the medicine. At follow up, resident reported the same level of moods and quality of life.	Escitalopram (discontinued)	N	Y
20	0	0	0	Prescribed escitalopram 20mg. However, behaviour is difficult to manage and has increased in difficulty, so not feasible to reduce or discontinue escitalopram	Escitalopram (continued)	N	N
21	0	0	0	Prescribed terazosin 2mg for severe incontinence. Not feasible to reduce or discontinue	Terazosin (continued)	N	N
22	0	0	0	Citalopram: Prescribed for depression. Moods have been stable over the past year. However, moods have deteriorated close to the assessment date. Therefore, GP* charted citalopram instead of moclobemide	All medicines continued	N	N
23	1	1	1	Temazepam: Prescribed 10mg. Initiated upon admission into the residential care facility. Has not had a previous trial of reducing or discontinuing temazepam. Therefore, suggested prescribing half a tablet (5mg) with the other half being prescribed 'as required. GP* agreed	Temazepam (reduced)	N	Y

				and resident tolerated the reduction well			
24	1	1	1	Amitriptyline: 10mg prescribed for an unclear indication. Resident prescribed several other sedative medicines for pain control. Therefore, questioned the need for amitriptyline. Both resident and daughter voiced that amitriptyline is probably not needed. Therefore, suggested tapering then discontinuing amitriptyline. GP* agreed. However, resident complained of increased insomnia and GP* re-prescribed it	Amitriptyline (reduced, discontinued, then re-prescribed)	Y	N
25	1	1	1	Citalopram: Reduced citalopram from 20mg to 10mg over three months and eventually discontinued this medicine as the resident tolerated the reduction well. However, the patient's moods deteriorated and re-prescribing of citalopram was necessary.	Citalopram (reduced, discontinued, then re-prescribed)	Y	N
26	1	1	1	Sertraline: Initiated upon admission into the residential care facility approximately 1 year and a half years prior to assessment date. Resident has settled into the residential care facility and moods stable. Suggested slow tapering and discontinuation. GP* agreed and resident tolerated this well.	Sertraline (discontinued)	N	Y
27	1	0	1	Deprescribing zopiclone is not feasible as they had recently lost their spouse and had been unsettled.	All medicines continued	N	N
28	1	1	1	Terazosin: Resident recently had an in-dwelling catheter (IDWC) inserted, so deprescribed terazosin	Terazosin (discontinued)	N	Y
29	1	0	1	Escitalopram: Resident suffers from bipolar disorder. Prescribed multiple antidepressants. Resident had scored 3 on the geriatric depression scale (<5: not depressed) at the time of assessment. Therefore, suggested monotherapy antidepressant therapy to the GP* by reducing escitalopram. However, resident suffered from an episode of bipolar low shortly afterwards, and it was not suitable to deprescribe escitalopram	All medicines continued	N	N
30	1	1	1	Clonazepam: Prescribed 0.5mg BD* for an unclear indication. Resident reported increased sedation during the day. Therefore, recommended trialling a reduction of this medicine to help improve resident's level of sedation.	Clonazepam (reduced)	N	Y
31	0	0	0	All medicines prescribed are clinically appropriate and required medically. No deprescribing recommendations put forward.	All medicines continued	N	N
32	1	1	1	Codeine: Prescribed 60mg BD*. Suggested reducing codeine dose to 30mg BD. GP agreed. However, resident experienced increased pain from stoma and codeine was increased.	Codeine (reduced, then increased)	Y	N
33	1	1	1	Escitalopram: Resident prescribed 20mg of escitalopram with no clear indication. Resident scored 3 on geriatric depression scale suggesting no active depression and reports good moods. Suggested trialling the reduction of escitalopram. GP* agreed and resident tolerated this well.	Escitalopram (reduced)	N	Y
34	1	1	1	Escitalopram: Indication unclear. Resident reports good moods and scored 2 on the geriatric depression scale. Discussed with resident and resident's daughter the need to continue escitalopram and they both agreed to a trial of reduction. GP* agreed with the recommendation. Escitalopram was reduced over three months and eventually discontinued.	Escitalopram (discontinued)	N	Y
35	1	1	1	Tramadol: On multiple sedatives, in addition to paracetamol and gabapentin. Reviewed the need for tramadol given the complex medicine regimen. Discussed this with the resident and resident's family who agreed to reducing tramadol. GP* agreed. Resident tolerated this well and eventually tramadol was discontinued.	Tramadol (discontinued)	N	Y
36	0	0	0	Unable to implement any deprescribing recommendations as resident passed away due to a myocardial infarction on 10/08/2016, before the date of the initial assessment	All medicines continued	N	N
37	1	0	0	Sertraline: Recommended slow tapering of sertraline as moods have been stable. However, moods deteriorated shortly after assessment and deprescribing was not feasible	All medicines continued	N	N

38	1	1	1	Citalopram: Prescribed for an unclear indication. Resident scored 2 on geriatric depression scale and reports good moods. Spoke to resident and son who agreed to a trial of deprescribing. GP* agreed. Resident tolerated reduction well and citalopram was discontinued.	Citalopram (discontinued)	N	Y
39	1	1	1	Codeine: Prescribed high doses of codeine for shoulder/hip pain. Suggested to GP* to increase regular paracetamol use for more effective pain relief and gradually taper codeine use. Resident tolerated this well and no longer needed higher doses of codeine.	Codeine (reduced)	N	Y
40	1	1	1	Alprazolam: Prescribed 500mcg of alprazolam TDS* for severe anxiety/post-traumatic stress disorder for over 15 years after the sudden loss of loved ones. Suggested to resident the gradual reduction of alprazolam. Resident and GP* agreed with this suggestion. Alprazolam 250mcg TDS* was prescribed regularly along with 250mcg TDS* as required, in case the resident needed it during the first few weeks of reduction. Resident tolerated the reduction well and did not request alprazolam as required.	Alprazolam (reduced)	N	Y
41	1	1	1	Ropinirole: Prescribed with no clear indication. Resident and GP* agreed to stop ropinirole. Patient tolerated this well.	Ropinirole (discontinued)	N	Y
42	1	1	1	Clonazepam: Resident prescribed 0.5mg three years ago after an outburst of aggression. Resident's mood had settled and no further acts of aggression have occurred. Therefore, suggested discontinuing clonazepam. GP* agreed and resident tolerated this.	Clonazepam (discontinued)	N	Y
43	0	0	0	Suffers from hallucinations and severe insomnia. Therefore, not feasible to deprescribe any target medicines (zopiclone, olanzapine)	All medicines continued	N	N
44	1	0	1	Quetiapine: Resident suffers from dementia. Quetiapine prescribed for no clear indication. Resident's moods have been stable according to family members and staff and agree to trialling a reduction. Therefore suggested gradual tapering of quetiapine and discontinuation. However, GP* did not agree with this suggestion. No clear reason was given as to why GP* disagreed with this recommendation	All medicines continued	N	N
45	0	0	0	Citalopram: Recently admitted into hospital for acopia before being transferred to the residential care facility, where he was prescribed citalopram. Therefore, was not suitable to deprescribe citalopram	All medicines continued	N	N
46	1	0	1	Zopiclone: Prescribed 7.5mg for the past ten years. Resident reports that zopiclone doesn't improve their sleep greatly. Therefore, suggested slowly tapering zopiclone to half a tablet regularly and half a tablet as required. However, GP did not agree. No clear reason was given as to why GP disagreed with this recommendation	All medicines continued	N	N
All residents	52	37	43				

GP: General practitioner; Y: Yes; N: No; BD: Twice daily; SR: Sustained release; mane: morning; TDS: Three times a day;

Colour	Meaning
	Deprescribed medicines were not represcribed
	Deprescribed but medicines were represcribed
	One or more medicines were successfully deprescribed (discontinued or reduced)
	GP trialled deprescribing; but medicines had to be represcribed

Deprescribing recommendations were not taken up by the GP, or the clinical situation of the resident changed; deeming them unsuitable to implement

Table 3: Outcome measures three months after deprescribing

Outcome	Statistical test	Effect size	P value
Primary outcome			
DBI	WSR*	Median: 0.09	p<0.001
DBI prn	WSR	Median: 0	0.41
Secondary Outcomes			
UKU-SERS score:	WSR	Median: 3.5	p <0.05
Psychiatric	Paired t-test	Mean: -1.83 95% CI= -2.62;1.00	p <0.001
Neurological	WSR	Median: 1.5	p <0.001
Autonomic	WSR	Median: 0	0.009
Other	WSR	Median: 1	p<0.001
UKU-SERS score: Adverse drug reactions	Paired t-test	Mean: -2.82 95% CI= -4; -1.64	p<0.05
Improbable	Paired t-test	Mean: -1.22 95% CI= -2.09; -0.26	p=0.01
Possible	WSR	Median: 1	p<0.05
Probable	WSR	Median: 1	p<0.05
Cognitive Performance Score 2	WSR	Median: 0	0.29
Geriatric Depression Scale	WSR	Median: 0.9	p<0.05

*WSR: Wilson-Signed Rank Test

Table 4: Outcome measures six months after deprescribing

Outcome	Statistical test	Effect size	P value
Primary outcome			
DBI	WSR*	Median: 0.34	p<0.001
DBI prn	WSR	Median: 0	0.16
Secondary Outcomes			
Regular Medicines	Paired t-test	Mean: -2.13 95% CI = -4; -1.71	P<0.05
PRN Medicines	WSR	Median: -0.5	0.16
Quality of Life	WSR	Median: 0	0.74
Frailty	Paired t-test	Mean: -1.35 95% CI=-2.22: -0.48	
Number of falls	WSR	Median: 0	0.04
UKU-SERS score:	WSR	Median: -5.5	p <0.05
Psychiatric	Paired t-test	Mean: -2.24 95% CI= -3.63; -1.12	p <0.001
Neurological	WSR	Median: -2	p <0.001
Autonomic	WSR	Median: -1	p <0.001
Other	WSR	Median: -1	p<0.001
UKU-SERS score: Adverse drug reactions	Paired t-test	Mean: -4.24 95% CI= -5.66; -2.83	p<0.05
Improbable	Paired t-test	Mean: -0.31 95% CI=-2.05; -0.26	p=0.52
	WSR	Median: -3	p<0.001
Possible	WSR	Median: -2	p<0.001
Probable			
Cognitive Performance Score 1	WSR	Median: 0	0.9
Cognitive Performance Score 2	WSR	Median: 0	0.6
Geriatric Depression Scale	WSR	Median: -2	p<0.05
Proportion of recommendations taken up by GPs	Fisher's exact test		p<0.05

*WSR=Wilcoxon signed ranked test

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